UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/402,488	02/16/2000	MAURICE MOLONEY	9369-98	6010

1059 7590 07/12/2006

BERESKIN AND PARR
40 KING STREET WEST
BOX 401
TORONTO, ON M5H 3Y2
CANADA

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/402,488	MOLONEY ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,12-16,18,19 and 48-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,12-16,18,19 and 48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1, 4-10, 12-16, 18-19, and 48-51 are pending in the application.

[2] Applicant's amendment to the claims, filed on 4/21/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Receipt of a Declaration under 37 CFR 1.132 by inventor Maurice Moloney, filed on 4/21/2006, is acknowledged.

[4] Applicant's arguments filed on 4/21/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, Second Paragraph

[6] Claims 4 and 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

[a] Claim 4 recites the limitation "said aspartic protease of step c)." There is insufficient antecedent basis for this limitation in the claim. In the interest of advancing prosecution, it is suggested that applicant change "c)" to "d)."

[b] Prior to amendment, claims 48-49 were drawn to the method of claim 1, whereby the contacting step occurred via co-expression of the recombinant protein and the aspartic protease in the host cell. However, claim 1 has been amended to require that the fusion protein be first obtained from the host cell prior to contacting with an aspartic protease. Thus, claims 48-49 have been interpreted as meaning that the fusion protein is obtained from the host cell and then, according to claims 48-49, the step of contacting is "effected by expressing said aspartic protease in said host cell." Claims 48-49 are confusing as it is unclear as to how applicant intends for the fusion protein, which is obtained from the host cell in step c), to re-enter the host cell for the contacting step to occur with a co-expressed aspartic protease. Alternatively, if one considers that the fusion protein is secreted from the host cell, it is unclear as to how the fusion protein, if co-expressed with an aspartic protease, is not cleaved by the co-expressed aspartic protease prior to obtaining the fusion protein from the host cell. It is suggested that applicant clarify the meaning of claims 48-49.

Claim Rejections - 35 USC § 112, First Paragraph

[7] Claims 1, 4-10, 12-16, 18-19, and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. This is a new matter rejection and is necessitated by amendment.

Addressing the amendment to claim 1 (claims 4-10, 12-16, 18-19, and 48-50 dependent therefrom), the claim has been amended to recite "transforming a *non-human* host cell" (emphasis added). MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims." Although applicant fails to show support for the "non-human host cell" limitation in claim 1, it would appear that, based on applicant's showing of support for newly added claim 51, applicant intends for p. 7, lines 3-4 of the specification as showing support for this limitation. Page 7, lines 3-4 of the specification discloses, "fusion proteins can be expressed in bacterial cells..., insect cells..., yeast cells, plant cells or mammalian cells." By amendment, the claim introduces a negative limitation to exclude a human host cell from the claimed method. Regarding such limitations, MPEP § 2173.05(i) states, "[a]ny negative limitation or exclusionary proviso must have basis in the original disclosure" and that "[a]ny claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement." Thus, while the specification would appear to support the method of claim 1, wherein the host cell is a bacterial, insect, yeast, plant, or mammalian host cell, it would not appear to support a limitation that excludes all a human cell. Applicant is invited to show support for the limitation at issue.

Addressing claims 48-49, prior to amendment, claims 48-49 were drawn to the method of claim 1, whereby the contacting step occurred via co-expression of the recombinant protein and the aspartic protease in the host cell, which was supported by

the original specification (see paragraph bridging pp. 12-13). However, claim 1 has been amended to require that the fusion protein be first obtained from the host cell prior to contacting with an aspartic protease. Thus, claims 48-49 have been interpreted as meaning that the fusion protein is obtained from the host cell and then, according to claims 48-49, the step of contacting is "effected by expressing said aspartic protease in said host cell." In view of the amendment to claim 1, the examiner can find no support for claims 48-49 in the specification. Applicant is invited to show support for claims 48-49 in the original application.

[8] The scope of enablement rejection of claims 1, 4-10, 13-16, 19, and 48-50 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. In view of the amendment to claim 1, namely to require that the fusion protein be obtained from the non-human host cell, claims 12 and 18 are included in the instant rejection for reasons noted below. Also, newly added claim 51 is added to the instant rejection. Thus, claims 1, 4-10, 12-16, 18-19, and 48-51 are rejected.

RESPONSE TO ARGUMENT: Applicant argues that by amendment, the claims no longer read on gene transfer in a human, but in a non-human host. Applicant argues that the specification discloses working examples of the claimed method in an *E. coli* host and further argues that the attached references support predictable and developed methods for recombinant expression of proteins in non-human host organisms, namely animals, bacteria, insects, and plants at the time of the invention. According to

applicant, the cited references demonstrate that the full scope of the claimed invention was enabled at the time of the invention.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification, while being enabling for a method comprising the steps of: transforming an isolated host cell with an expression vector as set forth in the claims, growing the cell to produce the fusion protein, obtaining the fusion protein from the cell, and contacting the fusion protein with an aspartic protease as encompassed by step d), optionally wherein the fusion protein is fed to an animal and the contacting of the fusion protein with the aspartic protease is in the stomach or gut of the animal, does not reasonably enable all methods as encompassed by the claims.

The examiner acknowledges applicant's amendment to exclude a human or a human cell as the host for fusion protein expression. There is no dispute that the fusion protein as set forth in the claims could be recombinantly produced in a bacteria, yeast, or insect cell at the time of the invention without requiring undue experimentation. However, claim 1 broadly encompasses recombinant fusion protein expression in *any* non-human host and claim 51 broadly encompasses recombinant fusion protein expression in *any* plant, not just those that are disclosed in the references cited by applicant in support of an enabling disclosure. At the time of the invention, the ability to conduct gene transfer in any animal or any plant was highly unpredictable.

Regarding gene transfer in animals, Dyck et al. (*Trends Biotechnol* 21:394-399, 2003) teaches that "the generation of transgenic domestic animals is difficult and often considered a barrier to their application" for recombinant protein expression (p. 396, left

column, bottom) and that "current methods of generating transgenic animal founders are relatively inefficient and time-consuming, and attempts to improve transgenesis by various methods have had limited success" (p. 396, left column, middle). Regarding gene transfer in plants, Vain et al. (*Theor Appl Genet* 105:878-889, 2002) teaches "transgene expression in plants remains largely unpredictable" and Potrykus (*Biotechnology* 8:535-542) teaches that gene transfer in cereals is largely unsuccessful and even the so-called "successful method" has problems (p. 535, right column, top). It should be noted that the references of Dyck et al. and Vain et al. were published well after the time of the invention. Thus, contrary to applicant's assertion that methods for generating a transgenic animal or plant for recombinant protein expression is neither predictable nor well-established as evidenced by the above cited references. In this case, the specification fails to disclose even a single working example of the claimed method in an animal or plant as broadly encompassed by the claims and it appears that none of applicant's cited references teaches recombinant fusion protein expression in an animal or plant as encompassed by the claims. While methods for generating a transgenic animal for recombinant protein expression were known in the art at the time of the invention as evidenced by applicant's cited references, a skilled artisan would recognize – particularly in view of the references of Dyck et al., Vain et al., and Potrykus – that it would require undue experimentation to make *all* transgenic animals and plants to practice the methods as encompassed by the claims.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It should be noted that, although the examiner has indicated enabled subject matter, this is no indication that such is supported by the instant specification, claims, and drawings as originally filed.

Claim Rejections - 35 USC § 103

[9] The rejection of claim(s) 1, 4, 6-9, 13, 15, and 19 under 35 U.S.C. 103 (a) as being unpatentable over Ward et al. in view of Walsh et al. and Yonezawa et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. Claim 51 is included in the instant rejection. Thus, claims 1, 4, 6-9, 13, 15, 19, and 51 are rejected.

RESPONSE TO ARGUMENT: Applicant argues the rejection is based on the incorrect assumption that chymosin will cleave any fusion protein at a Phe-Met junction. Applicant refers to the Moloney Declaration, which explains that the prior art references of Visser et al., which is cited by Walsh et al., and Schettenkerk et al., which is cited by Visser et al., disclose that a minimum chain length of five amino acids residues including a Ser-Phe-Met-Ala is required for cleavage of a κ-casein polypeptide. Applicant also points to the Moloney Declaration explaining that in Figures 1 and 2 and

the working examples that chymosin cleavage occurred between a Phe-Val and a Phe-Ser bond, respectively. In view of this evidence, applicant asserts the Moloney Declaration, the prior art, and the application data demonstrate that chymosin does not cleave all Phe-Met bonds. According to applicant, because one of ordinary skill in the art would not have expected chymosin to cleave all fusion proteins at a Phe-Met bond, the cited references fail to teach the claimed invention.

Applicant's argument is not found persuasive. It is noted that applicant is arguing against a limitation that is not present in the claims – the examiner cited Phe-Met as a representative example of a likely fusion site between a chymosin pro-peptide and a recombinant protein of interest. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

There appears to be no dispute that Ward et al. teaches a chymosin pro-peptide, which has Phe at its C-terminus, as a cleavable linker sequence of a fusion protein, Walsh et al. teaches the use of chymosin for cleavage of a fusion protein at a Phe-Met junction, and Yonezawa et al. teaches that chymosin *can* cleave, among others, a peptide having a Phe-Met junction. Applicant's position appears to be that chymosin does not cleave at all Phe-Met bonds. The examiner does not dispute applicant's assertion. However, that the prior art teaches that chymosin does not cleave at any Phe-Met junction does not by itself obviate the instant rejection.

At the time of the invention, the prior art regarding preferred cleavage sites for chymosin was well-developed as evidenced by the references of Yonezawa et al. and

Walsh et al. and also by references cited by Walsh et al., namely those of Visser et al. and Schettenkerk et al. Thus, if a direct fusion of a chymosin pro-peptide fused to a recombinant protein of interest is not amenable to cleavage by chymosin, one of ordinary skill in the art, in view of the available known cleavage sites for chymosin as taught by the prior art, could have readily engineered a cleavage site for a chymosin pro-peptide fused to a recombinant protein of interest with an expectation of successfully cleaving the pro-peptide from the recombinant protein of interest, particularly in view of the successful cleavage at a Phe-Met junction as shown by Walsh et al. and Yonezawa et al. Even applicant acknowledges that such experimentation was routine in the art at the time of the invention. In the response filed on 1/27/2003, applicant asserted that it is routine in the art to select a pro-peptide from any aspartic protease, fuse that pro-peptide to any recombinant protein of interest, and use any aspartic protease to cleave at the fusion protein junction (response filed on 1/27/2003 at pp. 3-5). As such, one of ordinary skill in the art would have had a reasonable expectation of success for fusing a chymosin pro-peptide to a recombinant protein of interest having an appropriate chymosin cleavage site and using chymosin to cleave at the fusion protein junction.

At least for the reasons of record and the reasons stated above, the examiner maintains the position that the claimed invention would have been obvious to one of ordinary skill in the art at the time of the invention.

[10] The rejection of claim 5 under 35 U.S.C. 103 (a) as being unpatentable over Ward et al. in view of Walsh et al. and Yonezawa et al. as applied to claims 1, 4, 6-9, 13, 15, 19, and 51 above, and further in view of Fine et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the combination of Ward et al., Walsh et al., and Yonezawa et al. fail to teach or suggest the claimed invention and the reference of Fine fails to remedy this failure.

Applicant's argument is not found persuasive. At least for the reasons set forth above, the examiner maintains that the references of Ward et al., Walsh et al., and Yonezawa et al. teach the invention of claims 1, 4, 6-9, 13, 15, and 19 and in view of the additional teachings of Fine et al., the invention of claim 5 would have been obvious to one of ordinary skill in the art at the time of the invention.

[11] In view of applicant's amendment to claim 1 to require that the fusion protein be obtained from the host cell prior to cleavage, which, according to claims 48-49 occurs by "expressing said aspartic protease in said host cell," the rejection of claims 48-49 under 35 U.S.C. 103 (a) as being unpatentable over Ward et al. in view of Walsh et al. and Yonezawa et al. as applied to claims 1, 4, 6-9, 13, 15, and 19 above, and further in view of Ward et al. (2) and LaVallie is withdrawn. The combination of references fails to teach the claimed method. See the rejection under 35 U.S.C. 112, second paragraph.

[12] Claim(s) 10 and 16 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Ward et al. in view of Walsh et al. and Yonezawa et al. as applied to claims 1, 4, 6-9, 13, 15, 19, and 51 above and further in view of evidentiary references Huber (US Patent 4,180,559) and Fan (US Patent 4,774,183). The rejection is necessitated by the amendment to claim 1 to require that the fusion protein be isolated prior to cleavage. Claims 10 and 16 limit the conditions for cleavage of the fusion protein to *in vivo* conditions. It should be noted that the claims are not limited to cleavage *in vivo* cleavage, but to cleavage under *in vivo* conditions. It should also be noted that the *in vivo* conditions are not limited to any particular organism and have been interpreted as encompassing a combination of *in vivo* conditions from more than one organism.

Ward et al., Walsh et al., and Yonezawa et al. disclose the teachings as described at pp. 11-12 of the Office action mailed on 12/30/2005. Particularly, Walsh et al. teaches cleavage of the fusion protein at pH 4.0 at 25 degrees Celsius (p. 237, right column). The cited references fail to teach cleavage of a fusion protein under *in vivo* conditions.

The references of Huber and Fan are cited to show that the conditions under which Walsh et al. cleaves the fusion protein are inherently *in vivo* conditions. Huber teaches, "[i]t is well documented that the pH of the [human] stomach contents can vary from 1.5 to 4" (column 1, lines 59-61), thus the *in vivo* pH of human stomach is 4. Fan teaches culturing of a fungus at 25 degrees Celsius (columns 4-6, Examples 1-4), thus, the *in vivo* temperature of the fungal culture is 25 degrees Celsius. Therefore, claims 10

and 16, drawn to the methods as described above would have been obvious to one of ordinary skill in the art.

RESPONSE TO ARGUMENT: Applicant argues there is no teaching or motivation in the prior art to use a mature aspartic protease to cleave a recombinant protein of interest. According to applicant, the teachings of Ward et al. (2) and LaVallie fail to provide a reasonable expectation of success of the claimed method.

To the extent applicant's argument is directed to the teachings of Ward et al., Walsh et al., and Yonezawa et al., the examiner maintains that this combination of references teaches the invention of claims 1, 4, 6-9, 13, 15, 19, and 51 at least for the above stated reasons. Regarding applicant's argument addressing the combination of Ward et al., Walsh et al., Yonezawa et al., Ward et al., and LaVallie, as the rejection no longer relies on the teachings of Ward et al. (2) and LaVallie, applicant's argument is moot.

[13] The rejection of claims 14 and 50 under 35 U.S.C. 103 (a) as being unpatentable over Ward et al., Walsh et al., and Yonezawa et al. as applied to claims 1, 4, 6-9, 13, 15, 19, and 51 above and further in view of Dunn et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the combination of prior art fails to teach the claimed invention. Applicant argues that, although mature aspartic proteases have been shown to cleave specific peptides at specific sites, this does not

implicate the use of a mature aspartic protease for cleaving the recited fusion protein. Applicant maintains the position that the rejection is based on hindsight reasoning because a skilled artisan would not expect that a fusion protein as recited in the claims could be cleaved by an aspartic protease without also incurring undesired cleavage. Applicant argues that without an assurance of accurate cleavage, there would have been no motivation to use an aspartic protease to cleave the fusion protein.

Applicant's argument is not found persuasive. As noted above, the invention of claim 1 is obvious in view of the combination of Ward et al., Walsh et al., and Yonezawa et al. and in view of the teachings of Dunn et al., the invention of claims 14 and 50 is obvious. In view of the combined teachings of the cited references, one of ordinary skill in the art would have had a *reasonable* expectation of success that chymosin can cleave its own fusion protein when fused to a recombinant protein of interest. While applicant maintains that one would not know whether chymosin would non-specifically cleave a fusion protein and one would not expect to achieve accurate cleavage, the claims are not limited to specific or accurate cleavage of a fusion protein. As such, applicant is arguing a limitation that is not present in the claims. See MPEP 2145 regarding arguing limitations that are not claimed. In this case, it appears that applicant's current argument appears to contradict applicant's previous statements of record, which clearly support non-specific cleavage of the fusion protein being encompassed by the claimed method. For example, applicant has previously argued that "the claims do not preclude some non-specific cleavage of the heterologous protein" (response filed on 9/18/2001 at p. 6, bottom). In the same response, applicant

states, "[a]pplicant has tested many proteins and has not observed *substantial* non-specific cleavage of any of the proteins" (italics added for emphasis, response filed on 9/18/2001 at p. 7, top), thus suggesting that at least *some* non-specific cleavage has been observed.

MPEP 2143.02 makes clear that absolute predictability is not required, only *some* degree of predictability. In view of the teachings as described above, one of ordinary skill in the art at the time of the invention would have had at least *some* degree of predictability that the fusion protein as taught by Ward et al. could be cleaved by an autocatalytically maturing aspartic protease other than chymosin, *e.g.,* pepsin, particularly in view of the teachings of Dunn et al.

Conclusion

[14] Status of the claims:

- Claims 1, 4-10, 12-16, 18-19, and 48-51 are pending.
- Claims 1, 4-10, 12-16, 18-19, and 48-51 are rejected.
- No claim is in condition for allowance.

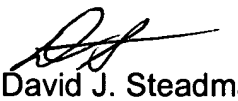
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656